UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/314,161	05/19/1999	MICHAL EISENBACH-SCHWARTZ	EIS-SCHWARTZ	4767

1444 7590 03/08/2004

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/314,161	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-62* is/are pending in the application.

4a) Of the above claim(s) *48, 53-54, 56, and 61-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47,49-52,55 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *47-62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 27 August 2003 has been entered in full. Claims 1-46 are cancelled and claims 47-62 are added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Newly submitted claims 48, 53-54, 56, and 61-62 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims are basically drawn to a method of causing activated T cells to accumulate at the site of neuronal degeneration by administering an effective amount of a NS-specific antigen or an immunogenic or cryptic epitope thereof. The newly submitted claims also recite that an individual is suffering from a disease that has neurodegenerative effects. However, the elected invention recites the administration of NS-specific activated T cells (25 April 2001) and injury (not disease) was elected as a species (14 September 2001).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 48, 53-54, 56, and 61-62 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's continued traversal of the Restriction requirement set forth in the communications of 14 June 2001 and 28 February 2001 appears moot since the restriction requirement was made final in the previous Office Action of 05 December 2001. If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144.

Claims 47, 49-52, 55, 57-60 are under consideration in the instant application as they read upon the elected invention of administering NS-specific activated T cells (25 April 2001) and the elected species of injury (14 September 2001).

Withdrawn Objections and/or Rejections

1. The objection to the specification at pg 4 of the previous Office Action (27 March 2003) is *withdrawn* in view of the title of the specification (27 August 2003).

2. The objection to claims 1, 2, 19, and 38-41 at pg 4 of the previous Office Action (27 March 2003) is *withdrawn* in view of the cancelled claims (27 August 2003).

Double Patenting

3. The rejection of new claims 47, 49-52, 55, 57-60 under the judicially created doctrine of obviousness-type double patenting as set forth for claims 1, 2, 19, and 38-41 at pg 4 of the previous Office Action (27 March 2003) is maintained and held in abeyance until all other issues are resolved. However, Applicant is encouraged to submit a terminal disclaimer at Applicant's earliest convenience.

New Non-Statutory Double Patenting

4. Claims 47, 51-52, 55, and 59-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43, 55-56, 79, and 82-83, of copending Application No. 09/765,644. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '644 application and the instant application recite a method of causing T cells activated against a nervous system (NS)-specific antigen to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease,

ameliorating the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '644 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claim in Application No. 09/765,644.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 47 and 55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47 and 51 of copending Application No. 09/765,301. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '301 application and the instant application recite a method of causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease, ameliorating the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '301 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claim in Application No. 09/765,301.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 47, 49-52, 55, and 57-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 32, 35-36, 44, 46, 48, 51-52, and 60-61 of copending Application No.09/893,344. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '344 application and the instant application recite a method of causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease, ameliorating the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '344 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claim in Application No. 09/893,344.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

New Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg.*

Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 47-52, 55, and 57-60 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 45-50, 53, and 55-58 of copending Application No. 09/893,348. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

8. Claims 47, 49-52, 55, 57-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) a method of reducing secondary neuronal degeneration in the central nervous system (CNS) or peripheral nervous system of an individual suffering from the degenerative effects of spinal cord injury or blunt trauma comprising intraperitoneally administering to an individual in need thereof a composition consisting of activated T cells sensitized to myelin basic protein (MBP) wherein the MBP-activated T cells accumulate at the site of injury or blunt trauma to reduce secondary neuronal degeneration, does not reasonably provide enablement for a method of reducing neuronal degeneration caused by the neurodegenerative effects of disease, or for reducing secondary neuronal degeneration that follows the primary neuronal damage of an injury, in the central or peripheral nervous system of an individual in need thereof, comprising: causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration in the individual in need, thereby reducing

neuronal degeneration at that site. The specification is also not enabling for a method for ameliorating the effects of an injury or disease that causes neuronal degeneration of the central or peripheral nervous system of an individual in need thereof, comprising causing T cells activated against a NS-specific antigen to accumulate at the site of neuronal degeneration in the individual in need, thereby ameliorating the effects of the injury or disease at that site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 4-10 of the previous Office Action (27 March 2003) and at pg 6-9 of the Office Action of 05 December 2001 for originally filed claims 1-2, 4-8, 16, and 19.

The claims also recite that the individual in need is one suffering from an injury that has caused primary neuronal damage.

Applicant's arguments (27 August 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant indicates that Prof. Schwartz made a comprehensive presentation (interview of 26 June 2003) explaining why predictions made in the present specification have been proved to be accurate. Applicant asserts that so many embodiments of the specification have been successfully tested that it would no longer be unexpected that the full scope of the present invention would work as disclosed. Applicant contends that it would not take undue experimentation to make and use the invention with respect to other NS-specific peptides or other neurodegenerative diseases or injuries.

Applicant's arguments have been fully considered but are not found to be persuasive. Undue experimentation would still be required of the skilled artisan to determine what other NS-

specific antigens and in the instant case, what peptides derived from NS-specific antigens, could be used to activate T cells and reduce neuronal degeneration, secondary neuronal degeneration, or ameliorate the effects of an injury or disease that causes neuronal degeneration. Relevant literature teaches that about 200,000 distinct mRNA sequences are thought to be expressed in the brain alone (a component of the central nervous system) and that this diversity results from the greater number and variety of cell types in the brain as compared to cells in the more homogeneous body tissues (pg 49, ¶ 1; Schwartz, J., "Synthesis and Trafficking of Neuronal Proteins", Principles of Neural Science, Connecticut: Appleton and Lange, 1991, pages 49-65). Schwartz states that the three membrane systems which constitute separate compartments within the neuron are made up of different proteins and serve separate functions within the cell (pg 50). Schwartz also continues to explain that a nerve cell makes three general classes of proteins: cystolic, nuclear/mitochondrial/peroxisomal, and cell membrane/secretory (pg 50-55). Therefore, due to the large quantity of proteins/antigens present in the central nervous system alone, the present invention is also unpredictable and complex wherein one skilled in the art may not necessarily reduce any kind of neuronal degeneration in the central nervous system or ameliorate the effects of injury or disease that causes neuronal degeneration comprising administering T cells activated against all possible NS-specific antigens. Since the specification also provides no guidance regarding what type of analogs of the NS-specific antigen and analogs and derivatives of the peptide should be utilized for the desired activity, the skilled artisan must resort to trial and error experimentation to determine which class of compounds might yield one with the desired activity.

Furthermore, the specification of the instant application fails to provide any guidance for the successful treatment of any injury, disorder, or disease other than spinal cord injury or blunt trauma using the claimed method. The scope of the claims encompass a method of reducing neuronal degeneration caused by the neurodegenerative effects of disease, a method for reducing secondary neuronal degeneration that follows the primary neuronal damage of an injury, and a method for ameliorating the effects of an injury or disease that causes neuronal degeneration of the central or peripheral nervous system of an individual. The scope of the claims encompasses diseases and injuries not expected to be commensurate with the elected species of injury, such as Alzheimer's disease, Huntington's disease, prion diseases, stroke, surgery, etc. (pg 44, ¶ 2). The effects encompassed by these diseases are broad and may include for example, memory loss, cognitive deficits, behavioral changes, and dementia, which effects are not commensurate with spinal cord injury. The etiology and pathology of spinal cord injury and blunt trauma is largely dissimilar from other diseases and injuries (particularly of the CNS) and the skilled artisan would not be able to predict that administration of NS-specific activated T cells would be beneficial for all possible diseases and injuries. The skilled artisan would also not be able to predict that administration of T cells activated against a NS-specific antigen would also cause NS-activated T cells to accumulate at the site of neuronal degeneration.

It is also noted that a broad, reasonable interpretation of the claims encompasses such diseases and injuries as Alzheimer's disease, Parkinson's disease, and Huntington's disease, among others, which have proven to be recalcitrant to treatment in the art (see for example, Halliday et al., Clin Exp Pharmacol Physiol 27: 1-8, 2000; Steece-Collier et al., Proc Natl Acad Sci USA 99(22): 13972-13974, 2002; Feigin et al. Curr Opin Neurol 15: 483-489, 2002).

Specifically, the specification does not teach any methods or working examples that indicate a reduction or amelioration of "primary" neuronal degeneration caused or exacerbated by injury or disease in CNS by administration of NS-specific activated T cells to an individual. The specification teaches that "a catastrophic consequence of central nervous system injury is that the primary damage is often compounded by the gradual secondary loss of adjacent neurons that apparently were undamaged, or only marginally damaged by the initial injury"(pg 4, [0008]). The specification also discloses that "neurons in the central nervous system do not undergo spontaneous regeneration following an injury" (pg 5, [0009]). As echoed by Jackowski, it is well known in this unpredictable art that regeneration does not occur in the CNS either because processes fail to grow the necessary distance, they are in competition with other nearby neuronal processes not derived from the affected nerve, astrocytic scarring blocks axonal elongation, or because of misdirected axonal growth (e.g., see Jackowski, Brit J Neurosurgery 9: 303-317, 1995; specifically pgs. 309-310 and pg. 305, last ¶). Accordingly, because of the lack of guidance provided by the specification as to how one can rescue dead or dying cells instantaneously affected, for example, by a head injury or neurodegenerative disease, there is no nexus that merely administering T cells activated against a NS-specific antigen to an individual in need thereof can reasonably be extrapolated to successfully treat any human subject experiencing *"primary"* neuronal degeneration, as claimed, without undue experimentation to determine such. The examples in the specification of the instant application only indicate that the administration of MBP-specific T cells reduces *secondary* neuronal degeneration caused by spinal cord injury or blunt trauma (pg 53-54; pg 60-64).

Relevant literature teaches that damage to the CNS is severe and irreversible, in part because of the failure of central neurons to regenerate axons (Kandel et al., Principles of Neural Science. 1991. Connecticut: Appleton and Lange; pg 264-265). Schwab et al. also indicate that "tissue damage and functional losses after spinal cord lesion result from the initial injury, which is immediate and irreversible, and from the reactive cascade of subsequent secondary molecular and cellular processes" (Physiol Rev 76(2): 319-370, 1996; see pg 327, col 2). Schwab et al. also teach that the cascade of secondary processes is reflected in the sequence of pathological changes that take place at the lesion site within days to weeks and that are fairly independent of the nature of the primary injury (see pg 327, col 2). Therefore, one skilled in the art would not expect an inhibition of secondary degeneration to also treat primary degeneration because the art indicates the primary "insult" or degeneration is irreversible and the processes involved in secondary degeneration are separate from those of the primary injury.

(ii) Applicant indicates that there are numerous references which relate to the present invention and reviews the results of several of them. Applicant argues that these papers establish for the record what Prof. Schwartz was able to explain at the interview of 26 June 2003. Applicant submits that in light of all the experiments that have been done with respect to this invention, the full scope of the present would be expected to be operable. Applicant asserts that there is no reason to believe that undue experimentation would be involved in order to make and use the full scope of the present invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Any references which the Applicant wishes for the Examiner to review and make of record

should be supplied in the form of an Information Disclosure Statement pursuant to 37 C.F.R. § 1.98(a)(1) which requires a list of all patents, publications, or other information submitted for consideration by the Office. The list of references has been placed in the application file, but the information referred to therein has not been considered. Submission of the proper PTO-1449 form with copies of the references listed therein will be taken into due consideration by the Examiner. It is noted that the Examiner has previously considered a few of the references listed in the response of 27 August 2003 (for example, Moalem et al. (Nat Med 5(1): 49-55, 1999), Moalem et al. (J Neuroimmunol 106 : 189-197, 2000), Hauben et al. (Lancet 354 : 286-287, 2000), Hauben et al. (PNAS USA 98: 15173-15178, 2001, Hauben et al. J. Neurosci 20: 6421-6430, 2000). However, only the elected invention is being examined at this time. Until the elected invention is deemed allowable, the references are not pertinent. The references will be considered when allowable subject matter relevant to the elected invention is identified.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate all possible NS-specific activated T cells and reduce "primary" neuronal degeneration by administering all possible NS-specific activated T, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of administering any NS-specific T cells to an individual, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

9. Claims 47, 51-52, 55, 59-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 47, 51-52, 55, 59-60 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the administration of NS-specific activated T cells. The basis for this rejection is set forth for cancelled claims 38-39 at pg 10-11 of the previous Office Action (27 March 2003) and pg 9 of the Office Action of 30 July 2002.

Applicant's arguments (27 August 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

At page 20 of the Response, Applicant argues that one does not look to the claims to find out how to practice the invention they define, but to the specification. Applicant also argues that no essential step is omitted, as the only essential step is causing the T cells to accumulate at the site of neuronal degeneration. Applicant argues that the administration of NS-specific activated T cells is not essential step for causing T cells to accumulate at the site of injury. Applicant indicates that claim 49, which specifies that activated T cells are administered does not add a step to claim 47, but further defines the causing step.

Specifically, Applicant's arguments have been fully considered but are not found to be persuasive because it is inappropriate to read limitations in the specification into the claims. The claims must independently define the invention for which patent protection is sought. Therefore, the claims are still rejected as being indefinite because the claims do not recite a step which

causes the NS-specific activated T cells to accumulate at the site of neuronal degeneration. It is noted to Applicant that claims 47, 51-52, 55, 59-60 have been examined to the extent that they read upon the elected group of administration of NS-specific activated T cells.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
25 February 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER